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Withdrawal of application for the marketing authorisation of Dazluma (troriluzole hydrochloride monohydrate)

Biohaven Bioscience Ireland Limited withdrew its application for a marketing authorisation of Dazluma for the treatment of spinocerebellar ataxia genotype 3 (SCA3), an inherited brain disorder that affects coordination and balance.

The company withdrew the application on 24 March 2025.

What is Dazluma and what was it intended to be used for?

Dazluma is being developed as a medicine to be used in adults for the treatment of SCA3. During the assessment, the company applied to broaden the indication to include all forms of spinocerebellar ataxia. In spinocerebellar ataxia, nerve cells in the cerebellum (the part of the brain that manages movement and balance) become damaged and die. This results in progressive problems with coordination, speech, walking and balance.

Dazluma contains the active substance troriluzole hydrochloride monohydrate and was to be available as capsules to be taken by mouth.

Dazluma was designated an 'orphan medicine' (a medicine used in rare diseases) on 10 December 2021 for the treatment of spinocerebellar ataxia. Further information on the orphan designation can be found on the Agency's website.

How does Dazluma work?

The active substance in Dazluma, troriluzole hydrochloride monohydrate, is a pro-drug of riluzole. This means that it is converted in the body to its active form riluzole.

High levels of glutamate, a chemical that allows nerve cells to communicate with other cells, increases stimulation of receptors (proteins) in the cerebellum. This may increase levels of calcium in the nerve cells which can cause them to die. Troriluzole's mechanism of action in spinocerebellar ataxia is thought to reduce levels of glutamate at the connections between nerve cells. This may alter the hyperexcitability in the nerve cells (when the nerve cells become overly sensitive) in the cerebellum that help control balance and coordination.

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What did the company present to support its application?

The company presented data from a main study involving 218 adults with different forms of spinocerebellar ataxia, including SCA3, which compared Dazluma with placebo (a dummy treatment). The main measure of effectiveness was the change in the severity of symptoms, as measured using the functional scale for the assessment and rating of ataxia (f-SARA) after 48 weeks of treatment. The f-SARA measures a person's ability to do tasks that show how well they can control their movements and keep their balance. Scores range from 0 to 16 with higher scores indicating more severe ataxia. During the assessment, the company also presented real-world data from patients with spinocerebellar ataxia, comparing how the disease progressed in patients treated with Dazluma to patients who did not receive any treatment.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn by the company after the European Medicines Agency had evaluated the information from the company and prepared questions for the company. After the Agency had assessed the company's responses to the last round of questions, there were still some unresolved issues.

What did the Agency recommend at that time?

Based on the review of the data and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had some concerns, and its provisional opinion was that Dazluma could not have been authorised for the treatment of spinocerebellar ataxia.

As the findings of the main study did not show that Dazluma was more effective than placebo for the treatment of spinocerebellar ataxia, the Agency considered that no conclusions could be drawn from it. The company also compared the effectiveness of Dazluma with real-world data from untreated patients. However, the Agency considered that the results from this comparison were not valid as additional factors to those considered by the company for their analysis could have influenced the difference in disease progression between patients treated with Dazluma and untreated patients. Therefore, at the time of the withdrawal, the Agency's opinion was that the effectiveness of Dazluma for the treatment of spinocerebellar ataxia was not proven.

The company had applied for Dazluma to be designated as a new active substance, on the basis that the efficacy and safety of its active ingredient differ significantly from those of a medicine that is already authorised in the European Union (EU). The Agency considered that the company had not shown that the efficacy or safety of troriluzole hydrochloride monohydrate is significantly different to its active form, riluzole, which is already authorised for use as a medicine in the EU. Therefore, the Agency could not conclude that troriluzole hydrochloride monohydrate is a new active substance based on the information submitted at this time.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of the application, the company stated that they plan to generate additional data to support a new active substance status for troriluzole hydrochloride monohydrate and plan to submit a new application once these data are generated.

Does this withdrawal affect patients in clinical trials or compassionate use programmes?

The company informed the Agency that there are no consequences for patients in clinical trials using Dazluma. The company is starting compassionate use programmes.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.